

AMENDMENTS TO THE SPECIFICATION

Please replace the paragraph beginning at page 10, line 26 with the following rewritten paragraph.

B1 Several species are particularly contemplated. For example, the invention provides a nucleic acid molecule wherein said Hu-Asp polypeptide is Hu-Asp1, and said polynucleotide molecule of ~~4~~(a) comprises the nucleotide sequence of SEQ ID NO.1; and a nucleic acid molecule wherein said Hu-Asp polypeptide is Hu-Asp2(a), and said polynucleotide molecule of ~~4~~(a) comprises the nucleotide sequence of SEQ ID NO. 3; and a nucleic acid molecule wherein said Hu-Asp polypeptide is Hu-Asp2(b), and said polynucleotide molecule of ~~4~~(a) comprises the nucleotide sequence of SEQ ID NO. 5. In addition to the foregoing, the invention provides an isolated nucleic acid molecule comprising a polynucleotide which hybridizes under stringent conditions to a polynucleotide having the nucleotide sequence in (a) or (b) as described above.

Please replace the paragraph beginning at page 12, line 13 with the following rewritten paragraph.

B2 In one variation, the cells are collected and the critical peptide is the APP C-terminal peptide created as a result of the β secretase cleavage. In another variation, the supernatant is collected and the critical peptide is soluble APP, where the soluble APP has a C-terminus created by β secretase cleavage. In preferred embodiments, the cells contain any of the nucleic acids or polypeptides described above and the cells are shown to cleave the β secretase site of any peptide having the following peptide structure, P2, P1, P1', P2', where P2 is K or N, where P1 is M or L, where P1' is D, where P2' is A. In one embodiment ~~method of claim 111 where P2 is K and P1 is M~~ and in another embodiment ~~The method of claim 112 where~~ P2 is N and P1 is L.

Please replace the paragraph beginning at page 23, line 27 with the following rewritten paragraph.

B3 Figure 2: Figure 2 shows the nucleotide (SEQ ID NO: ~~3-5~~) and predicted amino acid sequence (SEQ ID NO: ~~4-6~~) of human Asp2(~~a~~)(b).

Please replace the paragraph beginning at page 24, line 1 with the following rewritten paragraph.

B4 Figure 3: Figure 3 shows the nucleotide (SEQ ID NO: ~~5-3~~) and predicted amino acid sequence (SEQ ID NO: ~~6-4~~) of human Asp2(a). ~~The predicted transmembrane domain of Hu Asp2(b) is enclosed in brackets.~~

Please replace the paragraph beginning at page 32, line 21 with the following rewritten paragraph.

B5 a purified polypeptide as described in either of the preceding two paragraphs that further lacks amino acids 395-429 of SEQ ID NO: ~~4-6~~, which constitute a putative alpha helical region between the catalytic domain and the transmembrane domain that is believed to be unnecessary for β -secretase activity;

Please replace the paragraph beginning at page 32, line 26 with the following rewritten paragraph.

B6 a purified polypeptide comprising an amino acid sequence that includes amino acids 58 to 394 of SEQ ID NO: ~~4-6~~, and that lacks amino acids 22 to 57 of SEQ ID NO: ~~4-6~~;

Please replace the paragraph beginning at page 33, line 1 with the following rewritten paragraph.

B7 a purified polypeptide comprising an amino acid sequence that includes amino acids 46 to 394 of SEQ ID NO: ~~4-6~~, and that lacks amino acids 22 to 45 of SEQ ID NO: ~~4-6~~; and

Please replace the paragraph beginning at page 33, line 4 with the following rewritten paragraph.

B8 a purified polypeptide comprising an amino acid sequence that includes amino acids 22 to 429 of SEQ ID NO: ~~4-6~~.

Please replace the paragraph beginning at page 49, line 29 with the following rewritten paragraph.

B9 Several interesting features are present in the primary amino acid sequence of Hu-Asp2(a) (Figure ~~2~~3 and SEQ ID No. 4) and Hu-Asp-2(b) (Figure ~~3~~2, SEQ ID No. 6). Both sequences contain a signal peptide (residues 1-21 in SEQ ID No. 4 and SEQ ID No. 6), a pro-segment, and a catalytic domain containing two copies of the aspartyl protease active site motif (DTG/DSG). The spacing between the first and second active site motifs is variable due to the 25 amino acid residue deletion in Hu-Asp-2(b) and consists of 168-versus-194 amino acid residues, for Hu-Asp2(b) and Hu-Asp-2(a), respectively. More interestingly, both sequences contain a predicted transmembrane domain (residues 455-477 in SEQ ID No.4 and 430-452 in SEQ ID No. 6) near their C-termini which indicates that the protease is anchored in the membrane. This feature is not found in any other aspartyl protease except Hu-Asp1.
